

Original Article

Post COVID-19 changes in the structure and function of the thyroid in patients with autoimmune thyroiditis with hypothyroidism

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Abstract

COVID-19 is a severe immunosuppressive disease that can cause changes in the clinical course of autoimmune diseases. Autoimmune thyroiditis (AIT) is no exception. It is relevant to study the features of the clinical course of existing AIT in the post-COVID-19 period. The work aims to study the changes in the structure and function of the thyroid in patients with AIT with subclinical and manifest compensated hypothyroidism who had moderate COVID-19. A total of 123 patients aged 21–49 with AIT with subclinical hypothyroidism – 43 (group 1, 12 of whom had moderate COVID-19) and manifest hypothyroidism in the stage of medical compensation – 80 (group 2, 32 of whom had moderate COVID-19). The duration of AIT ranged from 4 to 13 years. In all cases, upon inclusion in the study and 2 and 6 months after it, changes in the structure of the thyroid gland were studied according to ultrasound data, as well as its functional capacity and the degree of compensation of hypothyroidism according to the thyroid-stimulating hormone indicator. In all patients with AIT, COVID-19 caused the progression of structural changes in the thyroid within one of two variants of the ultrasound picture of thyroiditis – hypoechoic heterogeneous or pseudo micronodular. The hormone-producing function also changed: in 7 out of 12 patients of group 1 of the main subgroup, hypothyroidism changed from subclinical to manifest hypothyroidism in the postoperative period, and in all patients of group 2 of the main subgroup, a further decrease in hormone synthesis was noted. In the post-COVID-19 period, patients with AIT undergo a progression of structural changes in the thyroid gland and a decrease in the synthesis of thyroid hormones.

Keywords: COVID-19, autoimmune thyroiditis, hypothyroidism, thyroid gland structure.

Introduction

COVID-19 has a multifaceted effect on the organs and systems of the body. In this regard, the endocrine system, particularly the thyroid gland, is no exception [1]. Available publications indicate that COVID-19, as a severe immunosuppressive disease, can exacerbate existing autoimmune diseases of the thyroid and changes in its function [2, 3]. So, it is relevant to study the features of the clinical course of AIT in the post-COVID-19 period [4]. The importance of such research is also evident because the incidence of AIT covers about 10% of the world's population, and adequate and timely cor-

rection of changes in thyroid status in patients with COVID-19 is vital.

Among the publications devoted to the impact of COVID-19 on the thyroid, this issue is the least covered. Worthy of attention is the work in which the results of the examination of more than 3,700 patients with COVID-19 in the United States were analyzed. The patients had AIT in the hypothyroid phase and had taken thyroid hormone drugs for a long time before COVID-19. The authors show that COVID-19 causes the progression of thyroid diseases and deepens its dysfunction, including hypothyroidism [5]. However, this conclusion needs to be clarified, in particular, it is worth



finding out what structural and functional changes in the post-COVID-19 period occur in patients with AIT with subclinical and manifests medically compensated hypothyroidism.

The work aimed to study the changes in the structure and function of the thyroid in patients with AIT with subclinical and manifest medically compensated hypothyroidism who had moderate COVID-19.

Material and methods

A number of 123 women with normotrophic AIT were examined. The age of the patients is from 19 to 49 years. The duration of the disease was from 4 to 12 years. According to the severity of primary hypothyroidism, patients were divided into two groups: subclinical hypothyroidism and manifest hypothyroidism, compensated for euthyroidism with toroxine drugs. In each group, two subgroups were made: main and control. The main subgroups consisted of patients who suffered from moderate COVID-19 and consulted an endocrinologist after 2–3 months due to worsening of the general condition. Control subgroups include patients who did not suffer from COVID-19. The patients in the selected groups and subgroups were identical in terms of age and duration of the disease.

Upon inclusion in the study and 2 and 6 months after it, all patients underwent a general clinical examination and sonography of the thyroid gland to study the changes in its structure, the level of antibodies to peroxidase (IU/ml) and hormonal function according to the TSH indicator (mU/l) were determined [6, 7]. The results obtained after 2 and 6 months were compared with each other and with the values at the time of admission to the study (Table 1). It should be noted that, according to the initial data, TSH and TPOAb lev-

els were higher in patients of the main subgroups compared to patients of the control subgroups ($p < 0.05$).

We also considered changes in the dose of thyroxine replacement therapy as one of the indicators of the functional capacity of the gland in the synthesis of hormones.

Results and discussion

The main reason for the patient's appeal was the deterioration of the general condition and the increase in symptoms of the existing AIT. Patients suffered from deterioration of their general condition, pain, pressure or sensation of a foreign body on the front surface of the neck, chills, drowsiness, and weight gain. During the examination, a dense, moderately painful thyroid gland, dry skin, and normo- or bradycardia were found in all persons. This symptomatology was characteristic of exacerbating the clinical course of AIT or deepening hypothyroidism. Other authors also note in their reports the aggravation of the clinical course of existing AIT after suffering from COVID-19 [8, 9].

According to ultrasonography 2 months after having COVID-19, the structure, size and volume of the thyroid gland, compared to the initial data, did not change significantly in patients of both groups.

A deterioration of thyroid parenchyma structure was noted within the limits of the hypoechoic and heterogeneous variant of the ultrasound picture of chronic thyroiditis 6 months after having COVID-19 in patients with subclinical hypothyroidism, compared to the data at the time of inclusion in the study (Figure 1 A). It was manifested by an increase in the intensity of lymphocytic infiltration of the thyroid parenchyma, and in three of them, isolated hypoechoic foci of the "Swiss cheese" type appeared (Figure 1 B).

Table 1: Distribution of patients and initial data of the studied values.

Group of patients	Subgroup of patients	Age	Duration of the disease with AIT	TSH	TPOAb	Dose of thyroxine
Subclinical hypothyroidism (n=43)	Main (n=12)	38.23±4.61	5.24±2.02	4.97±0.45*	653.2±21.71*	0
	Control (n=31)	37.71±4.07	5.37±1.17	5.71±0.27	327.8±19.43	0
Manifest hypothyroidism (n=80)	Main (n=32)	39.27±3.12	7.25±1.87	6.49±0.31*	594.9±13.35*	64.47±2.15
	Control (n=48)	36.18±2.73	6.41±1.72	3.12±0.19	299.8±14.12	62.47±0.91

Note: * – changes are reliable in comparison with values in the control group. Digital data were processed statistically using the MsExcel 2010 program.

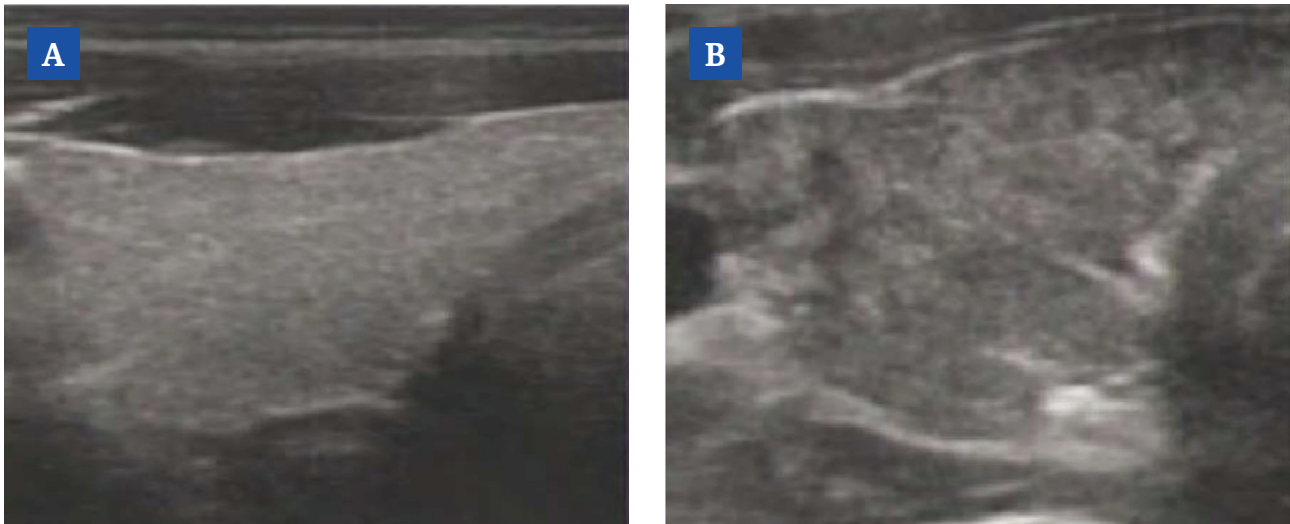


Figure 1: Echocardiogram of the thyroid: A – normal variant; B – structural changes according to the hypoechoic and heterogeneous variant with single hypoechoic foci (patient V., 39 years old, suffering from AIT for 8 years).

In patients of both subgroups with manifest hypothyroidism (group 2), when included in the study, multiple loci of focal changes typical for the pseudo micronodular variant were structurally determined (Figure 2). At the same time, changes of the “Swiss cheese” type (small pseudomicronodules on the background of the predominant parenchyma) were found in 25 patients of the control and 19 patients of the main group, and of the “honeycomb” type (small merging pseudomicronodules on the background of connective tissue and a small amount of parenchyma) in 23 of the control group and 13 of the main group (Figure 2 A, B).

During the examination after 6 months, the structural changes of the thyroid parenchyma did not change in the patients of the control subgroup. An increase in the intensity of lymphocytic infiltration and the number of loci of focal changes was noted in all patients of the main subgroup. As a result of these processes, the frequency of the “honeycomb” type increased from 13 to 21. Such a structural reorganization of the thyroid parenchyma against the background of already existing changes indicates that COVID-19 stimulates the course of autoimmune processes and the deepening of structural changes in the thyroid. A number of authors

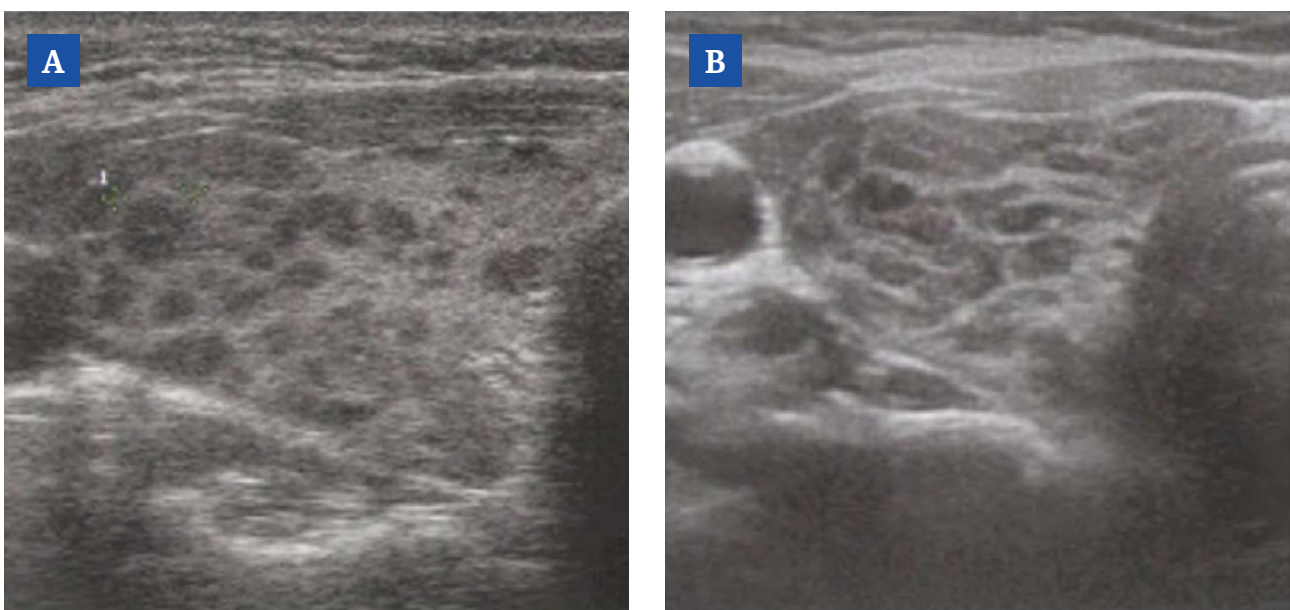


Figure 2: Echocardiogram of the pseudo micronodular variant of structural changes in the thyroid of patients with AIT: A – patient H., 28 years old, has been suffering from AIT for 7 years, structural changes similar to the “Swiss cheese” type; B – patient M., 32 years old, suffering from AIT for 8 years, structural changes like “honeycombs”.

also reported on the progression of structural changes in the thyroid after having COVID-19 [8–10]. However, they should have classified them according to the ultrasound picture’s variants, making it difficult to assess the prolongation of the process.

The thyroid function was determined in patients of both groups at inclusion in the study after 2 and 6 months after observation. In patients of the control subgroups, during these periods, changes in TSH values occurred within the limits of euthyroidism. As for the main subgroups of patients, significant changes in the hormone-producing function of the gland should be noted.

Thus, in patients of group 1 of the main subgroup, the TSH value changed during the indicated periods. In the second month of observation, the TSH level in four patients decreased by 2–4 mU/l within the limits of euthyroidism compared to the values at the time of examination. Such changes in TSH levels can be explained by the activation of destructive processes in the gland, which is also evidenced by the results of sonography and the TPOAb level. After six months, manifest hypothyroidism with TSH levels ranging from 9 to 13 mU/l was clinically and laboratory determined in seven patients, which required compensation with thyroxine replacement therapy (Table 2).

The patients of group 2 in the main subgroup before COVID-19 had manifested hypothyroidism in the stage of medical compensation. Two months after COVID-19, against the background of the use of thyroxine drugs in the previous dose, in 9 patients, TSH was within the reference values, and in 23 it was elevated and determined in the range from 6.5 to 15.7 mU/l, which indi-

cated a decrease in thyroid hormone production and an insufficient dose of thyroxine. The dose of replacement therapy was increased individually by 25–50 µg/day for these patients. During the control study of TSH for the adequacy of the dose of replacement therapy in 17 of them, its level was within the limits of euthyroidism, and in 6, it was elevated, which indicated an insufficient dose of thyroxine and the need for its repeated correction. Study 6 months after COVID-19 showed that in 6 patients among 9, who in two months, TSH had within the reference values clinically and laboratory diagnosed hypothyroidism with TSH levels from 8.3 to 12.7 mU/ml. In this regard, the dose of replacement therapy was increased. In the remaining patients of this group, the level of TSH was within the limits of euthyroidism (Table 1).

TPOAb levels in patients of the control subgroups did not change reliably during the observation period and ranged from 254 to 357 IU/ml. In patients with subclinical and manifest hypothyroidism, when examined 2 months after inclusion into the study, compared with the initial indicators, the level of TPOAb was higher, but the changes are unreliable. In the 6th month of observation, the level of TPOAb in all patients of both groups of the main subgroups decreased, and in general, this decrease was reliable across groups (Table 2).

The results of the conducted studies showed that COVID-19 significantly affects the clinical course of autoimmune thyroiditis. It causes the progression of structural changes in the thyroid parenchyma, an increase in the level of antibodies to thyroperoxidase and changes in its hormonal function. In patients with subclinical hypothyroidism, a temporary decrease in

Table 2: Indicators of thyroid function, antibodies to thyroid peroxidase and thyroxine dose after COVID-19 in patients with AIT.

Group of patients	Thyroid peroxidase, a thyroid-stimulating hormone						Dose of thyroxine mcg/day	
	When taken for research		After 2 months		After 6 months		When taken for examination	After 6 months
	TSH	TPOAb	TSH	TPOAb	TSH	TPOAb		
Group 1, main subgroup (n=12)	4.97±0.45	653.2±21.71	3.48±0.79	685.4±24.71	7.31±1.93*	597.3±19.35*	0	49.32±4.36
Group 2, main subgroup (n=32)	6.49±0.31	594.9±13.35	9.45±0.49*	612.9±14.21	4.49±0.75*	511.7±12.35*	68.4±0.74	94.25±1.79*

Note: * – the difference is reliable compared to the data when taken for the study and after 2 and 6 months of observation.

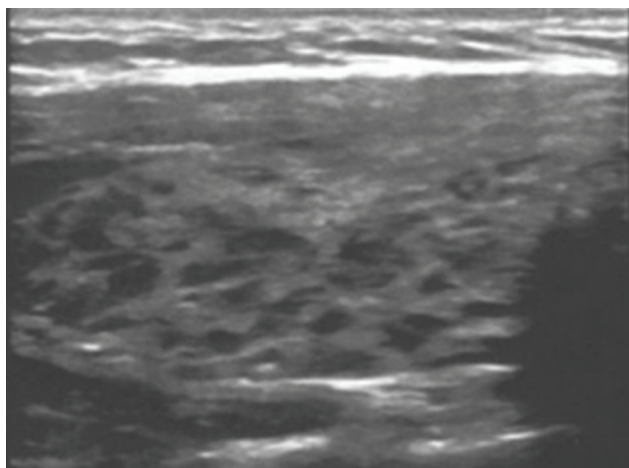


Figure 3: Patient N., 27 years old. Ultrasound of the thyroid gland before the COVID-19 disease. A pseudo-micronodular variant of the “Swiss cheese” type.

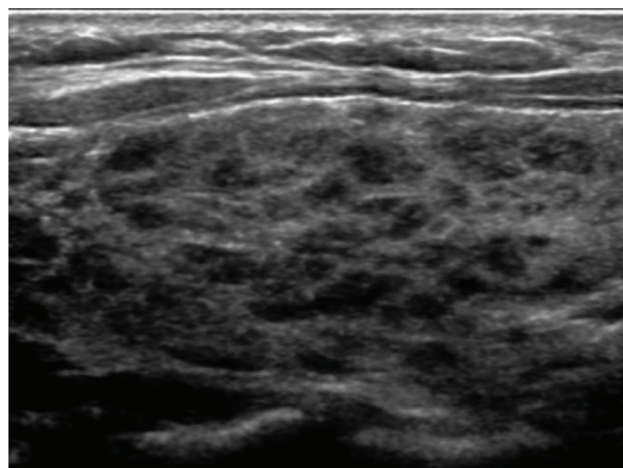


Figure 4: Patient N., 28 years old. Ultrasound of the thyroid gland after COVID-19 diseases. A pseudo-micronodular variant of the “honeycomb” type.

the level of thyroid-stimulating hormone and an increase in the level of TPOAb due to the activation of destructive processes in the thyroid within the hypoechoic heterogeneous type of structural changes can be observed. The progression of destructive processes in the thyroid is accompanied by a decrease in hormone synthesis and the transition from subclinical hypothyroidism to manifest hypothyroidism, and patients with manifest hypothyroidism require an increase in the dose of replacement therapy.

Here is a clinical case: Patient N., 27 years old, has been suffering from AIT for 7 years. Diagnosis: autoimmune thyroiditis, normotrophic form, manifest hypothyroidism, medical compensation. She received replacement therapy with Euthyrox at a dose of 75 µg/day for a year. From April, 15 to April 27, 2020, she was at the infectious department of the hospital because of a moderate pandemic coronavirus infection, where she was treated according to the clinical protocol. She did not stop taking Euthyrox. A month before COVID-19, she had a planned examination for AIT. There were no specific complaints then. The TSH value was 3.9 mU/l. Ultrasound results – a thyroid gland with a volume of 13.7 cm³, both lobes are symmetrical and multiple pseudo micronodules are determined against the background of infiltrated parenchyma. The specified changes were assessed as a pseudo micronodular variant of the “Swiss cheese” type (Figure 3).

She applied on July 2, 2020, concerning the deterioration of her general condition. She complained of fatigue, general weakness, drowsiness, chills, pain in the area of the front surface of the neck, which worsened when swallowing, hoarseness of voice and an increase in body weight by 5 kg. Palpation of the front surface of

the neck revealed slight tenderness. The skin is dry, the pulse rate is 62 bpm, the heart is rhythmic and the blood pressure is 125 and 65 mm Hg. Ultrasound – the parenchyma of the thyroid gland is infiltrated, heavy, with multiple “honeycomb” pseudomicronodules. Compared with data for March 2020, the thyroid volume did not change. Structurally, an increase in lymphocytic infiltration was noted. As of July 2, 2020, TSH is 9.8 mU/l, and TPOAb is 538 IU/ml. The dose of replacement therapy was increased to 100 µg/day. After 2 months after increasing the daily dose of Euthyrox, she was examined again. The general condition slightly improved, but fatigue and drowsiness continued to bother her. As of September 4, 2020, the level of TSH in the blood decreased to 5.3 mU/l and TPOAb – to 502 IU/ml. The dose of Euthyrox was adjusted to 112.5 µg/day. During the re-examination, 1.5 months later, the patient noted an improvement in her general condition; fatigue, drowsiness, and a feeling of cold disappeared. The heart’s activity is rhythmic at 76 bpm, blood pressure 120- and 70-mm Hg. According to ultrasound, a thyroid gland with a volume of 14.2 cm³, parenchyma with multiple strands, infiltrated, with pseudo micronodules in “honeycomb” type (Figure 4), TSH as of October 22, 2020, 2.7 IU/l, and TPOAb – 485 IU/ml.

Thus, structural changes of autoimmune genesis increased in the patient’s thyroid gland after COVID-19. As a result, the echo structure of the gland within the pseudo micronodular variant changed from the type of “Swiss cheese” to “honeycomb”. The result of these changes was a further decrease in the hormone-producing function of the thyroid and the progression of hypothyroidism. The patient was compensated for hypothyroidism by increasing the daily dose of Euthyrox.

Conclusion

COVID-19 affects the clinical course of autoimmune thyroiditis. It activates the progression of structural changes in the thyroid gland. Structural changes are accompanied by a decrease in hormone synthesis and aggravation of hypothyroidism.

Conflict of interest

The authors declare no conflict of interest.

Ethics approval

The approval for this study was obtained from the Ethics Committee of the Horbachevsky Ternopil National Medical University, Ternopil, Ukraine (approval ID: 123/21 - 21.09.2021).

Consent to participate

Written informed consent was obtained from the participants.

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